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Nd:YAG Interstitial Laser Thermotherapy in the Treatment of Breast Cancer

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Background and Objective: **"Minimal treatment strategy" is desirable in certain breast cancer patients. The main objective of the present study is to examine the use of interstitial laser thermotherapy (laserthermia) for this purpose.**
Study Design/Materials and Methods: **Thirty-five patients with primary breast cancer were treated with laserthermia using the Nd:YAG (1,064 nm) pulse-wave laser. In 28 patients, laserthermia was performed before radical resection, and in seven patients it was the only invasive treatment.**
Results: **One gaseous rupture of tumor occurred at 3 Watts. The diameter of single focus of laser-induced damage after 1–2 Watts was less than 1 cm, and after 2.5–6 Watts it reached 1.5–2.5 cm. Of seven patients treated without surgery, local tumor control was achieved in five, and in three stage I–III patients disease-free survival followed for 19–60 months. After laserthermia plus surgery, 3-year disease-free survival was 27% in premenopausal and 92% in menopausal patients.**
Conclusions: **It seems that laser destruction of relatively small primary breast cancer is possible. Provisionally, laserthermia should not be used in premenopausal patients. Lasers Surg. Med. 22:257–267, 1998.**

Key words: **cancer; infrared laser; infrared laser; complications; minimally invasive therapy**

INTRODUCTION

Some breast cancer patients of elderly age are denied combined modality therapy, because of coexistent disease or fears that they are unable to tolerate surgery or protracted courses of radiotherapy. The results of treatment with antiestrogen tamoxifen alone are poor [1]. The concerted effort to define optimal breast cancer therapy in the aging population includes the evaluation of alternative treatment approaches, such as radiation and tamoxifen (without excision). The desirable "minimal treatment strategy" would limit the surgery to the diagnostic puncture procedure, such as core biopsy or fine-needle biopsy, and to yield the acceptable rates of local control [2].

Interstitial contact Nd:YAG thermotherapy (laserthermia), the minimally invasive technique to produce local hyperthermia by the infrared ir-

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radiation through the fiber inserted into the middle of the tumor, was introduced by S.G. Bown in 1983 under the name of "photocoagulation" [3], and it has been shown to be capable of heating the tumor above the temperature levels of protein coagulation, and to produce irreversible tumor damage [4,5]. Laserthermia can be performed as an outpatient procedure, under ultrasound, CT, or MRI guidance, for ablation of human malignancies such as hepatic tumors [6,7], as well as in the treatment of cancer and benign hyperplasia of the prostate [8,9].

Our initial clinical experience has shown that Nd:YAG interstitial laser thermotherapy (ILT) is a technically simple procedure, has minor toxicities, and significant cytoreductive potential, and can be easily incorporated into the radiologic workup or treatment scheme in patients with breast cancer [10].

The aim of the present study, which has been underway since 1991 under the auspices of the Ministry of Health of Ukraine, is to examine the use of laserthermia in human primary breast cancer and to determine for this cancer localization a clinically safe and effective regimen. Study design included a preclinical phase, a clinical neoadjuvant phase I (assessment of tolerability), and a clinical conservative phase II (pilot study on effectiveness). In clinical phase I the laserthermia was applied to the tumor before the operation, as "neoadjuvant radiologic therapy." The reduction of tumor burden lowers the risk of tumor dissemination during the surgery, and the histological assessment of the treated tumor enables the fastest possible modification of the treatment dose [11].

MATERIALS AND METHODS

The preclinical phase of the study included computer simulation of the laserthermia, and the ex vivo ultrasound-guided laserthermia of 12 breast carcinomas resected with the whole breast.

A mathematical model was developed for computer simulation of laserthermia which takes into account the exponential absorption of infrared light in tumor tissue, the differing tissue blood flow at tumor layers and during heating, and the phase transitions during laserthermia (vaporization and condensation). The model is based on quasi-unidimensional equation of transient heat conduction with spherical symmetry of heating source distributed by volume. The equation is solved numerically on a personal computer using the technique of finite differences [12,13].

The ex vivo laserthermia experiments were conducted on mastectomied specimens immersed into a water tank at a temperature of 37°C. The temperature curves on needle thermocouple probes were registered during the laser irradiation with differing powers, and then data were entered into database for computer simulation. Also the accuracy of ultrasound-guided positioning of the fiber and of the thermocouple probes was assessed by inspection of these specimens cut through the carcinoma.

In clinical phase I, between the February 1992 and December 1993, in Kharkov Institute of Medical Radiology, 28 patients were treated with ILT, which was followed by surgical resection ("neoadjuvant laser treatment"). The diagnosis, size, and localization of tumors were established with clinical examination, ultrasonography, and fine-needle aspiration biopsy and confirmed by the histology of the mastectomied specimen. The median age of patients, all female, was 53 years (range 38–78 years), and the median tumor diameter was 3 cm (range 1–6 cm). Also during this period two patients entered into the conservative arm of the study (treatment of carcinoma with ILT without surgery). In neoadjuvant patients, the endpoints during short-term observation were 1) foci of laser destruction of tumor tissue, their histology and size, and 2) short-term systemic responses and adverse reactions, as assessed by clinical observation and laboratory tests.

The study protocol was approved by the Scientific Board of the Institute and by the Ukrainian Ministry of Health (Ethical Committees were established in the Ukraine in 1996). All the patients entered into the study on the basis of informed consent, after the experimental nature of ILT in the treatment of breast cancer, as well as limited knowledge on long-term effects of such treatment, were explained. Each patient entering the trial was treated with the maximum dose known to be safe at the time of administration.

In the first 20 patients in phase I, ILT was applied using the same power and exposure for each in subgroups of five patients. After the interim analysis of histologic and clinical data of such a series, the decision was made to increase the power level. This "stepwise dose escalation" [14] was started with 1 Watt, the minimal power claimed by some authors to be effective [15]. The data on foci sizes were entered into the computer

model. In the last eight patients of the "neoadjuvant" series and in seven patients of the "conservative" series, the ILT was conducted in feedback mode using the individualized treatment plans.

The histological technique used for the study of post-irradiation foci was described previously [16]. In some tumors, electron microscopy and tissue enzyme measurements were performed for the parallel analysis of tissue damage.

The laserthermia was performed 1–11 days before surgery (various times of resection were chosen to study how laser lesions evolve histologically in the short term), with contact Nd:YAG laser (Polar Ltd., Russia) in a pulse-wave mode (pulse repetition rate 20 Hz, pulse duration 100 μsec). The laser output optical system consisted of a lens focusing the laser beam of 8 mm diameter onto the fixed butt-end of a 400-μm quartz fiber. The opposite "patient's" end of fiber was stripped of its plastic cladding and cut plain. The laser power regulator (voltage supply to quantum generator) was calibrated by the power output at the "patient's" end of the fiber measured with calorimetric technique. The simplest design of fiber tip (bare, plain-cut) was chosen to guarantee the patient's safety (after the treatment session the used portion of fiber is cut off) without energy losses in delivery system, after the expert advice from Professor S.G. Bown (personal communication, May 17, 1990).

At the treatment session, under local anesthesia and with constant ultrasonographic visual control, the 18-gauge arteriovenous needle was inserted through the skin into the tumor, and via needle cannula the quartz fiber was positioned, so as to allow its bare tip to contact the tumor tissue. Two needle-shaped thermocouples were inserted in the periphery of the tumor, 1.0–2.0 cm from the middle of the tumor. Consecutive subgroups, of five patients each, were treated with 1 Watt, 2 Watts, 2.5 Watts, and 3 Watts. In the feedback mode, used in the last 15 patients, the laser power was controlled during the treatment session within the range of 2.5–6 Watts so as to raise the temperature in the thermocouples up to 50°–55°C and to hold it for 10–15 minutes.

The imaging modality used for the visualization of tumor and for guidance of instruments during the treatment session was high-resolution (7.5 MHz) real-time ultrasound sonography (ultrasound scanner TI 628A, Radmir Corporation, Kharkov).

The long-term follow-up of neoadjuvant patients was performed in order to analyze the impact of preoperative ILT on the disease-free survival. The clinical, laboratory, and radiologic check-up was conducted at least every 3 months. The interim statistical analysis of disease-free survival was performed using 1-year data, and final analysis using 3-year data.

After the analysis of long-term data from the "neoadjuvant" series, the indications and contraindications for further use of ILT in breast cancer have been detailed. After the publication of information on this study in national mass-media news bulletins [17], a number of patients were referred for ILT, and during the period from February to June 1995 five patients were selected and entered into the conservative arm of the study. In general, the conservative phase II of the study included seven patients in whom ILT was used as the only invasive therapy in their treatment scheme. The diagnosis was verified by pre-ILT histological needle "core" biopsy. In three stage IV patients, the ILT was intended for palliation, and in four stage I–III patients it was used as the alternative to surgery in the primary treatment. The conservatively treated patients were followed for 5–64 months, and regular check-ups included US or CT tumor measurements. In three patients during the follow-up period, ultrasound-guided "core" puncture biopsy of the tumor site was performed for suspected recurrence [16].

Data were analyzed by the chi-square test for comparing proportions, or the Student t-test for continuous variables. A value of $P < .05$ was considered significant. Disease-free rates were evaluated using the method of Kaplan and Meier [18].

RESULTS

Computer simulation has shown that, to achieve irreversible damage of tumor tissue with ILT, various levels of laser energy per unit of tumor tissue are required at different power settings. For example, the results of simulation for the deep-situated tumor of diameter of 2 cm, under the tissue blood flow of 6 ml/100 g/min, are as follows. Using a power setting of 2 Watts, the outer layers of tumor remain intact even after 8 kJ (approximately 1.9 kJ/cm^3); using 4 Watts the whole tumor is irreversibly damaged after 3.3 kJ (0.8 kJ/cm^3); and using 7 Watts the tumor is ir-

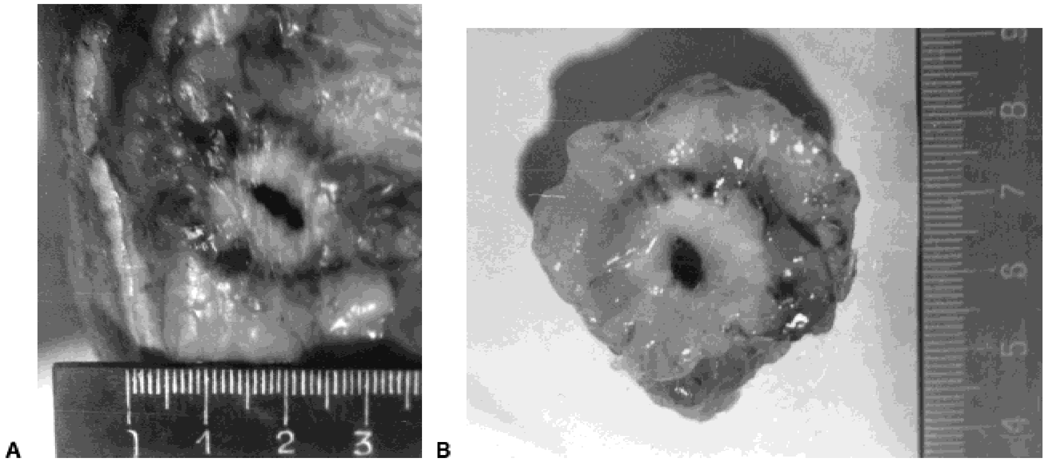


Fig. 1. Gross appearance of breast carcinomas with foci of laser-induced damage. Small black central cavity corresponds to the point of interstitial Nd:YAG laser irradiation. The main volume of focus is presented by extensive tissue infarction, red at periphery (dark rim on the photo), and discolored in the central portion exposed to temperatures above 50°C. Unstained specimens. Ruler indicates centimeters. **A:** Breast carcinoma resected 3 days after laser thermotherapy with 2.5 W, 3,000 J. **B:** Breast carcinoma resected 1 day after laser thermotherapy with 3–5 W feedback mode, 5,400 J.

reversibly damaged after 2.1 kJ (0.5 kJ/cm^3). At this stage of the study, the range of powers between 2.5 and 8 Watts was assessed as being of the most clinical potential. Meanwhile, the maximum tolerated power and energy of ILT for breast cancer, as well as dose-limiting toxicities and complications, requires determination in further clinical study.

In vitro ILT of mastectomied specimens demonstrated sufficient accuracy of ultrasound-guided positioning of fiber and of thermocouples (median deviation 2 mm, range 0–5 mm). In clinical study, after laserthermia, in approximately 50% of patients, minor toxicities were observed day 0 post-lasing. They included transient fever, nausea, and anxiety; no statistically significant link was established to power or energy of laserthermia. In patients treated with 1 Watt and 2 Watts, no other complications were observed. However, for the tumors referred (mainly 2.5–4 cm in diameter), these power settings were estimated as subadequate and the transition to higher power was decided.

In patient 17, after treatment with 3 Watts, 5,400 J, a complication regarded as serious, namely, gaseous rupture of the tumor, occurred. It manifested with sudden pain and subcutaneous emphysema. No other clinical symptoms were observed during 3 days of follow-up between the ILT and surgery.

Small skin burns (blisters) were observed in two "neoadjuvant" patients and in two "conservative" patients after lasing the tumor fixed to the skin with powers above 2.5 Watts, and energies of 8,500–23,600 J. Subclinical hyperfibrinogenemia during day 0 post-lasing, with peak levels of 4.2 and 4.4 g/liter was registered after 2.5 Watts, 7500 J, and after 2.5–3 Watts, 7,200 J, correspondingly.

At postoperative specimen inspection, in all the tumors clearly demarcated foci of laser-induced tumor destruction were revealed. Generally, the diameter of the entire focus is larger with larger power and exposure (Fig. 1a,b). In tumors lasered with 1 Watt and 2 Watts, the diameter of foci, at exposures up to 20 minutes, was less than 1 cm. After lasing with 2.5 Watts, 3 Watts, and in feedback (2.5–6 Watts) mode, the diameter of laser-induced foci was 1.5–2.5 cm. By superposition of number of foci it was technically and clinically feasible to cover the complete volume of tumor up to 3.5 cm in diameter.

The small central "core" (1–3%) of focus' volume consisted of a small evaporation cavity with a thin wall of carbonization, vacuolization, and necrosis (Fig. 2). The main volume of foci presents tissue infarction, discolored in the central area exposed to higher temperatures. Within the infarcted area, severely damaged cancer cells preserve at light microscopy the cell outlines, while by electron microscopy the membranes appear fragmented (Fig. 3a,b). At larger distances from the source of irradiation the degenerative features in cancer cells are presented by pycnotic nucleus with unclear boundaries and with no visible nucleoli (Fig. 4a,b). In tumors inspected 7–11

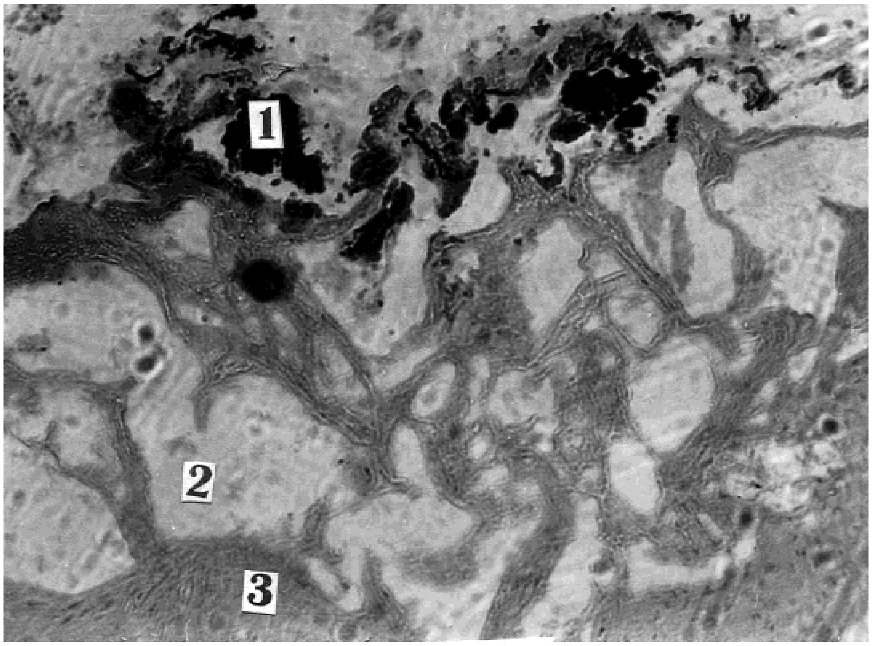


Fig. 2. Carbonization (*1*), vacuolization (*2*), and necrosis (*3*) of breast cancer tissue at 2 mm from the source of interstitial Nd:YAG laser irradiation. Day 1 after thermotherapy with 3 W, 1,800 J. Hematoxilin and eosin, ×100.

days after ILT, the fibroblastic activity is revealed at periphery, while the central area of the focus presents no significant dynamics.

At long-term follow-up after ILT plus surgery, during the period of observation (5–33 months) one patient out of 28 has died; the death occurred 2 months after surgery from a cardiac problem. The remaining 27 patients were alive with median follow-up of 22 months. Eight patients developed distant metastases during the period of observation. The median period from ILT and surgical treatment to the diagnosis of metastases was 20.5 months (range 7–26). There was one case of local disease recurrence; it appeared 14 months after ILT plus surgery (nonradical mastectomy) in a patient with a large tumor which suffered a gaseous rupture during the ILT (see above). Eighteen months after ILT plus surgery this patient also developed distant metastases. In rate of metastasis after treatment, no statistically significant difference was revealed when comparing "neoadjuvant" patients from this study with clinically equal patients from the pooled data on the same population, after the traditional combined treatment [19]. In the patients from present study, the pre-menopausal status was revealed to be the main prognostic feature for the development of distant metastases after the laserthermia plus surgery. Actuarial 3-year disease-free survival rate, calculated by Kaplan-Meier, was 27% for the premenopausal women, and 92% for the postmenopausal women.

In the conservative stage of clinical study the results are as follows.

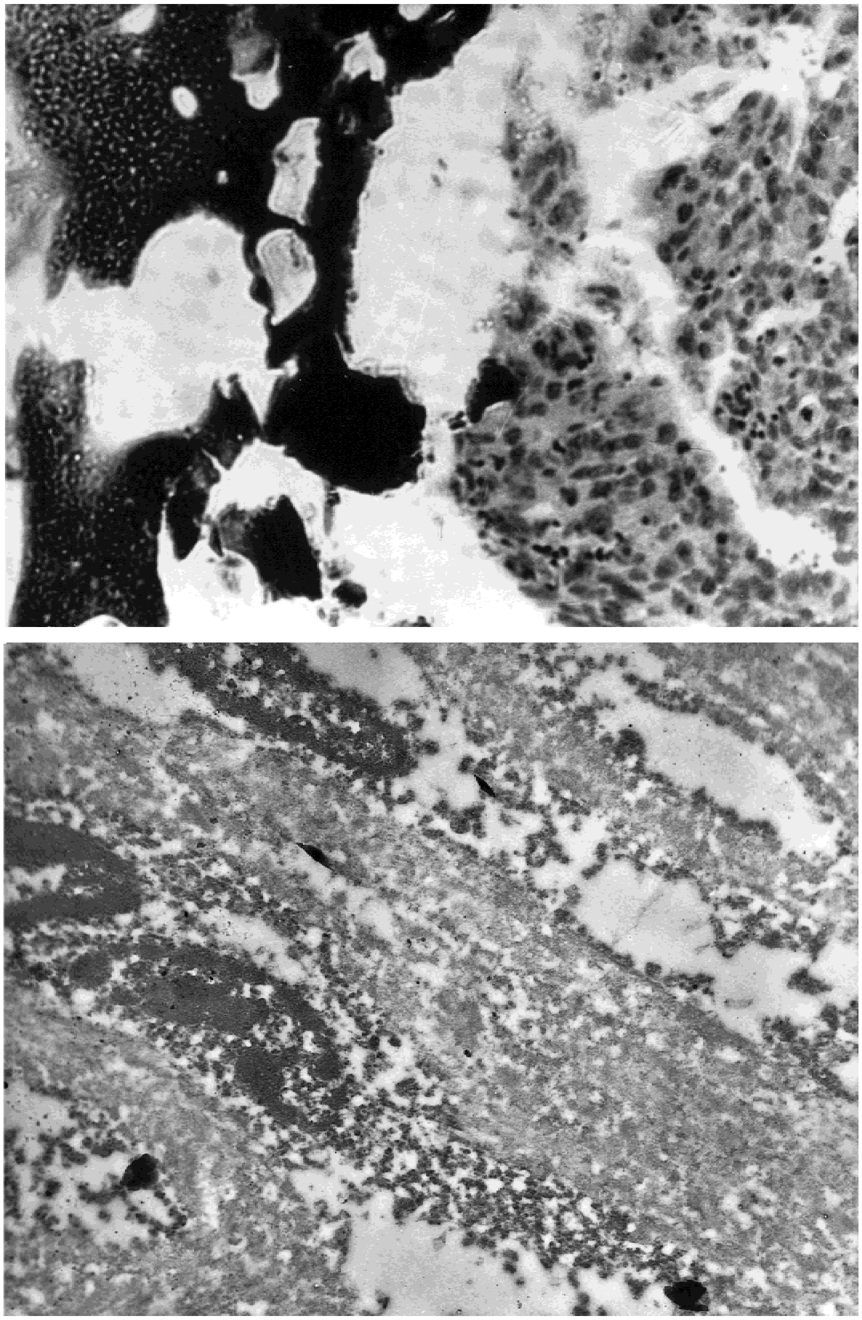
In all three postmenopausal patients with operable and borderline operable disease, a cytotoxic effect of ILT was observed, and the results were evaluated as promising, with regard to local tumor control and quality of life.

Case 1

In a 60-year-old stage I patient with concomitant rheumatism, mitral valve defect and supraventricular tachicardia, the primary tumor of diameter of 2.5 cm was treated with 1–5 Watts, 16.7 kJ. During the 2 months after ILT, the tumor shrank in volume by 80%, and no regrowth was observed during follow-up; "core" puncture biopsy yielded fibrotic tissue. The patient was active and assessed her result as "excellent." She died suddenly 19 months after ILT of progressive chronic heart failure.

Case 2

In a 68-year-old stage III patient with concomitant hypertension, coronary heart disease, and chronic pancreatitis, the primary tumor of 3 cm in diameter with skin fixation was treated with 1–5 Watts, 8.5 kJ. Burn of skin fixed to the tumor occurred during the treatment, with subsequent ulceration. The ulcer healed per secundam at 3 months; during this period the smears of



A

B

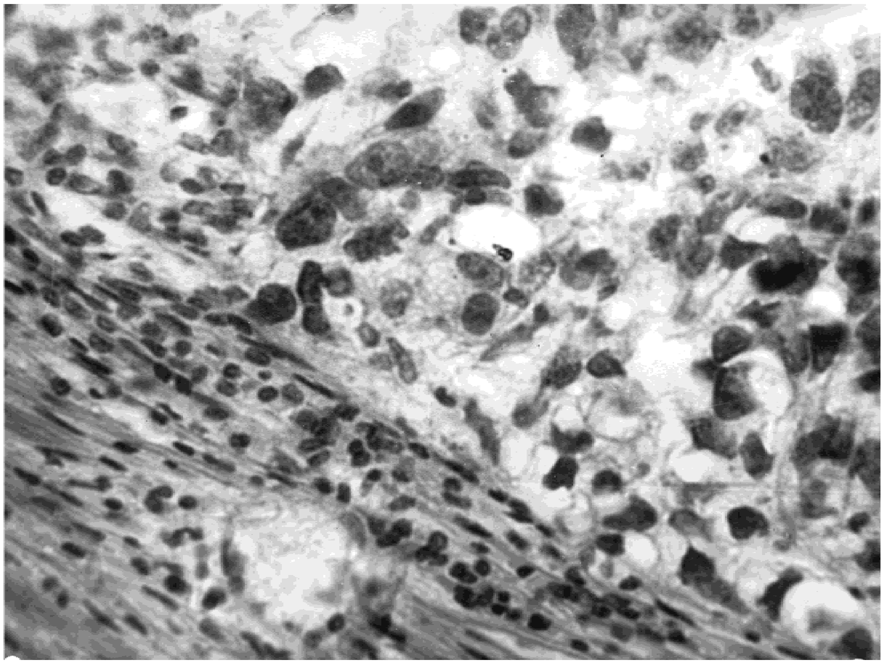
Fig. 3. Cluster of degenerate breast cancer cells preserving cell outlines borders the carbonized mass, at 4 mm from the source of interstitial Nd:YAG laser irradiation. Breast carcinoma resected 2 days after thermotherapy with 2.5 W, 2.250 J. **A:** Hematoxilin and eosin, ×200. **B:** Electron microscopy of the specimen of the same cancer tissue taken at the same distance reveals completely destructed cell membranes ("ghost cells"). ×40,000.

wound were taken 4 times, with no atypical cells revealed. At follow-up 20 months after ILT the patient was active, with no limitation to ipsilateral arm and no signs of disease recurrence.

Case 3

In a 78-year-old stage I patient with concomitant coronary heart disease, postinfarction cardiosclerosis, and bronchial asthma, the elongated primary tumor of size 3 × 2 cm was treated using 2 Watts, 4.8 kJ, which was followed by fractionated radiotherapy to breast (46 Gy). By day 40 after treatment, the tumor became nonpalpable and could not be detected at ultrasound sonography. During the follow-up period the patient was disease-free. She is alive and active and has recently completed (by April 1997) her 5-year survival term.

An operable premenopausal patient, after ILT (approximately 1.4 kJ/cm^3), presented no improvement in the quick progress of her disease.



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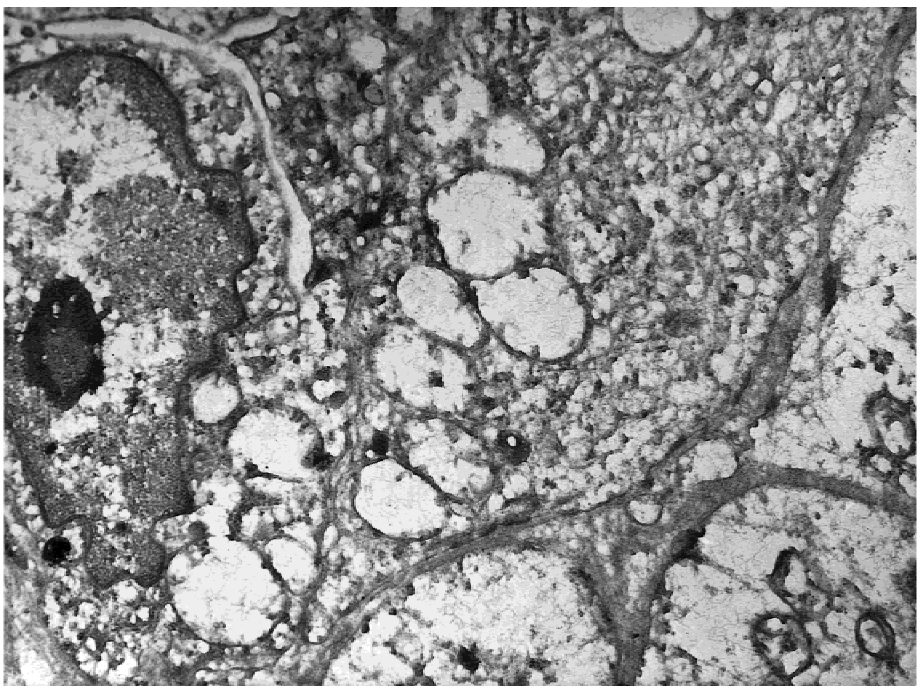

B

Fig. 4. Degenerative changes of breast cancer cells at the distance of 12 mm from the source of interstitial Nd:YAG laser irradiation. Breast carcinoma resected 5 days after thermotherapy with feedback 3.5–4.5 W, 6,300 J. **A:** Light microscopy presents damaged cancer cells with luminous cytoplasma and pycnotic nuclei. Hematoxilin and eosin, ×200. **B:** Electron microscopy reveals in cancer cell osmyophilia and numerous invaginations of nucleus' membrane, and mytochondria without crystae. ×40,000.

Case 4

A 34-year-old stage II patient self-referred for nonsurgical treatment of a tumor of 4 cm in diameter with pectoral fixation. She was categorized as noneligible for ILT and was strongly advised to consider mastectomy. Two months later, after chemotherapy and radiotherapy, she reappeared with tumor, diminished by size to 2.5 cm and insisted on being treated with ILT. The tumor was treated with 1–4.5 Watts, 11.2 kJ. At checkup by month 3 after ILT the tumor was regrowing, and "core" biopsy revealed fibrotic tissues containing viable cancer cells. Also swollen axillary nodes appeared, which required hormonotherapy. By month 5 she was lost to followup. It is unclear if there exists a pathophysiological link between ILT and the quick progress of the disease in this case.

In inoperable menopausal stage IV patients

who were treated using ILT with the intent of palliation, cytostatic effect was observed in two out of three cases.

Case 5

In a 54-year-old patient with distant metastases to the spine, a large primary tumor of 4 cm in diameter and with cancer infiltration of overlying skin was treated using 3–8 Watts, 23.6 kJ. Skin burn occurred. No certain positive changes were registered during the period of observation. She died 6 months after ILT of disease progression.

Case 6

In a 52-year-old patient with distant metastases to pelvic bone, within one session, using 2–4 Watts, the primary tumor of diameter of 3 cm was treated with 5.9 kJ, and the regional lymph node of diameter of 2 cm was treated with 1.7 kJ. During the initial period of observation, the primary tumor shrank in volume by 15%, and the node shrank in volume by 20%, with no regrowth. She died 13 months after ILT of metastases.

Case 7

In a 54-year-old patient with metastases to pleura, the flat primary tumor of size 4.5 × 3.5 × 2 cm was treated with 2–5 Watts, 15.0 kJ. Two months after ILT the main volume of tumor appeared necrotic at "core" biopsy, but regrowth was revealed at two points at the tumor periphery. She died 7 months after ILT of intoxication.

DISCUSSION

Laserthermia is a new technique of minimally invasive tumor ablation, with certain advantages when compared to RF-heating, cryoablation, or interstitial ethanol injection [20]. Theoretically, ILT has the potential to destroy breast tumors as an alternative to surgical lumpectomy [5,21,22], but no sufficient knowledge on regimens and dosages appropriate for human breast carcinoma and its different varieties, as well as on the long-term clinical consequences of such a therapy, is yet available.

Breast cancer is one of the leading causes of death in the female population in industrialized world [23], and breast screening programs are widely implemented resulting in an overwhelming number of nonpalpable lesions suspected to be cancer and presenting significant challenges to surgeons and radiologists [24]. The decision on treatment strategy involves questions of survival expectancy, risk of recurrence, cosmesis, and preservation of femininity. Innovative therapy, before sufficient data on effectiveness and safety are accumulated, carries some ethical risk, and the clinical study on laserthermia for breast cancer should be designed in such a way as to minimize this potential risk. In the present initial study, the clinical phase I, which lasted for 3 years, was devoted to the determination of maximal tolerable dose and of possible complications and contraindications to ILT, in a "neoadjuvant" framework. Human breast carcinomas were treated with contact Nd:YAG laser preoperatively, and the histological study of lasered tumor, inspected after operation, was used as the treatment endpoint. Subsequently these data regimens of laserthermia were modified so as to reach the optimal combination of clinical safety and effectiveness. In the next step, clinical pilot phase II, the regimens and dosages assessed as safe and effective, as well as a treatment planning program, have been applied in seven patients as the only invasive treatment.

In the initial series of phase I, one complication regarded as serious, the gaseous tumor rupture, occurred. At long-term follow-up in this patient, local tumor recurrence and distant metastasis were observed. To our knowledge, this is the first complication of that sort reported in ILT. After this case, we preferred not to enroll patients with tumors larger than 4 cm in diameter (since large tumors are known to have extended central areas of spontaneous necrosis) and to safeguard at the initial period of laserthermia session, so that the temperature rise in the tumor is not too steep.

At long-term follow-up, some patients who were treated using a combination of ILT with surgery have developed distant metastases. The main factors predictive of metastases occurrence were premenopausal state and younger age. While there was no statistically significant increase in disease recurrence, when compared to data from the same population receiving combination therapy without ILT, we propose, as a precaution, that further clinical studies on ILT for breast cancer should include only older postmenopausal patients.

At histological examination, when heating the breast carcinomas between 50°C and 55°C for 10–15 minutes, the single focus of laser-induced damage was 1.5–2.5 cm in diameter. To a limited extent, the superposition of several foci of laser-

thermia could be successful in the destruction of tumors of larger diameter. Those data are in good accordance with data of a study on breast cancer conducted in the United Kingdom at the same time [21]. In a series of 45 patients, authors report that foci of laser destruction in breast carcinoma reached a diameter of between 0 and 2 cm.

With laserthermia regimens similar to those in present study (5 Watts, 20 min), and with the temperatures of 45–65°C, lesions of identical size are reported in cancer lesions in liver [25–27]. In prostate cancer, lesions of very similar gross appearance to those observed in breast carcinoma after medium power and long exposure are reported after short exposures to high powers (40 W per 90 sec, or 60 W per 60 sec), but after these regimens the regrowth seems to be more frequent [8,9]. Possibly, in the near future, tissue-specific response rates for different malignant and benign tumors will be quantified from these clinical observations, interpreted in terms of "time-temperature isoeffect" concept [28,29].

After the potentially lethal photothermal laser damage, breast carcinoma presents at light microscopy controversial findings of viable-appearing cancer cells and of cells presenting mitotic figures [16] which are similar to the findings of "ghost cells" in liver metastases [30,31]. This controversy is partially resolved by electron microscopy and by immunochemistry stains, but the most certain assessment of tumor cell kill can be achieved by prospective observation of treated tumor in vivo. In our study, during the first 10 days, laser lesions in breast cancer presented very minimal histologic dynamics. This is in agreement with the observation on experimental animal tumors which have not evolved histologically for 36 days after lethal laser damage [32], and therefore prospective studies in humans should be months and years long.

The present study and a clinical study in the United Kingdom [21,22] seem to show that laser destruction of relatively small breast carcinomas is clinically and technically feasible. Laserthermia is relatively easily tolerated (minor toxicity) and could be combined with other nonsurgical modalities of breast cancer treatment (radiotherapy, chemotherapy, tamoxifen). In the present study, the visualization modality for guidance of laserthermia was high-resolution ultrasound. This technique is relatively cheap, and for the past decade it has been widely used as the standard approach in guided puncture needle biopsy of lesions in the breast as small as 6 mm [33–36]. The success rate is claimed to be 100% in experienced hands [37].

The advantage of ultrasound as a guidance modality is that it permits the "free-hand" puncture technique, does not require puncture needles other than standard, does not limit the room for surgical manipulation, and allows a comfortable position for the patient [38,39]. Meanwhile, ILT can also be implied with other radiologic modalities used for guided needle puncture of breast lesions, such as mammographic stereotaxic systems [40,41], or MRI [22,42,43]. The unique feature of MRI is its capability of direct monitoring of laser-induced necrosis and of the tissue temperature [9,22,25].

As we see it, the data available at the moment provide sufficient biological, clinical, and medico-ethical justification to propose a wider clinical trial on alternative primary treatment, using a combination of laserthermia with antiestrogen therapy (tamoxifen) and (if necessary) with radiotherapy, in selected postmenopausal women with stage I–II breast cancer who have contraindications to surgery and narcosis, or have strong aversion to surgery. To yield sufficient statistical power and provide the necessary data on complications and quality of life, as well as 5-year and 10-year disease-free survival figures broken down by the size of the lesions, by nodal extent of the disease, and by photothermal dose, such a trial should be organized as a cooperative multicenter effort. This future coordinated study will establish the "guarantee kill" photothermal dose and regimens for various subtypes of breast carcinomas (differing in photothermal cancer cell sensitivity, in cellularity, and blood flow) and could be conducted by several centers with whatever guidance modality they prefer.

ILT could also be tested in palliative treatment of some patients with advanced breast cancer and in recurrences of breast cancer (stages III and IV). "Sculpting" the temperature field to the tumor shape will be significantly eased by a multifiber approach [44] and by the use of elongated diffusers [45]. In some cases the inclusion of ILT into the individual treatment scheme of patients with advanced breast cancer will contribute to prevention of pain and minimization of disability. The physician treating such patients must be aware of all the alternatives and must select the most appropriate therapy or therapies for each patient with her particular set of circumstances [46].

In conclusion, the results of the present pilot

clinical study seem to provide some evidence that in certain situations interstitial laser thermotherapy can be a useful addition to traditional methods of breast cancer treatment.

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